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Case Report

Ex utero intrapartum treatment for extremely low birth-weight neonates requiring resuscitation at birth

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ABSTRACT

Objective: Difficulties often encountered during intubation in extremely low birth-weight (ELBW) neonates requiring resuscitation at birth because of the smaller airway and the pressure from the limited number of attempts before hemodynamic instability occurs.
Case report: We evaluated two pregnant women at 26 weeks of gestation with premature rupture of membranes and evidence of chorioamnionitis and applied the concept of ex utero intrapartum treatment, which involved delaying cord clamping (DCC) after establishing a secured airway with adequate ventilation during cesarean delivery. The resuscitative procedure was smooth and all three neonates had favorable outcomes at one month of age.
Conclusion: When cesarean delivery is indicated in ELBW infants and intubation after birth is anticipated, DCC after establishing a secured airway may help maintain neonatal cardiovascular stability and allow physicians to resolve the technical difficulties of intubation.

Introduction

In preterm infants with extremely low birth weight (ELBW, weighing <1000 g), resuscitation after birth is often required to maintain adequate gas exchange and hemodynamic stability, and it can be achieved by rapidly establishing a definite airway through endotracheal intubation. However, the smaller airway of an ELBW neonate compared to that of a term neonate and the pressure from the limited number of attempts before hemodynamic instability occurs are often difficulties encountered during intubation. Furthermore, the intubation process is associated with unfavorable physiologic changes, including increased intracranial pressure and rapid deterioration of heart rate and oxygen saturation [1]. Failed or prolonged intubation attempts can cause persistent adverse changes, leading to inadequate ventilation and oxygenation [2]. Consequently, ELBW infants frequently deteriorate during intubation attempts.

The ex utero intrapartum treatment (EXIT) procedure is primarily performed during cesarean section in cases where obstructive airway is anticipated at delivery due to oral or neck tumors. Delaying cord clamping keeps the neonate on placental circulation, which in turn allows time for surgical treatment during delivery. We assessed two pregnant women at 26 weeks of gestation with antepartum hemorrhage due to placenta previa totalis and premature rupture of membranes with evidence of acute chorioamnionitis. Preterm delivery was inevitable. Delayed cord clamping (DCC) after establishing a secured airway for ventilation was achieved by the EXIT approach during cesarean delivery. The resuscitative procedure was smooth and all three neonates had favorable outcomes at one month of age.

Case 1

Patient A was 31 years old, nulliparous and pregnant at 17 weeks of gestation with dichorionic twins via in vitro fertilization after ten attempts. Other than primary infertility, the patient had underlying hypothyroidism and received oral thyroxine sodium daily. She was referred to our hospital for placenta previa totalis with antepartum hemorrhage and intermittent lower abdominal pain of one-month duration. At admission, the laboratory data showed no subclinical infections: serum level of C-reactive protein (CRP), 1.9 mg/L (normal range, <5 mg/L) and white blood count, 4500/μL with segmented neutrophils of 74.4%. Normocytic anemia (hemoglobin,

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9.2 g/dL; mean corpuscular volume, 98.9%) was noted. Urinalysis was clean. Intravenous infusion of ritodrine was administered to treat uterine contractions, but was later changed to atosiban due to intolerable side effects. Intermittent vaginal bleeding was associated with uterine contractions throughout the hospitalization. At 25 3/7 weeks' gestation, watery discharge gushed from the vagina, and premature rupture of membranes was confirmed using a sterile speculum examination and positive results of an Actim PROM test (Medix Biochemica, Espoo, Finland). Consequently, betamethasone for accelerating fetal lung maturation and antibiotic therapy with intravenous infusion of ceftriaxone and metronidazole were administered. However, progressive turbid vaginal discharge and elevated CRP levels were noted (44.3 mg/L). Sonography at 26 weeks of gestation showed an estimated fetal weight of 788 g with no amniotic fluid for one fetus and 708 g with adequate amniotic fluid for the other fetus. Additionally, signs of several placental lacunae with diffused intraparenchymal lacunar flow were noted, suggestive of placenta accreta. Endocervical microorganism cultures obtained by sterile speculum examination were positive for Group D Streptococcus and *Acinetobacter nosocomialis*. Chorioamnionitis was confirmed, and termination of the pregnancy was indicated. Prompt cesarean delivery with DCC using the EXIT method was suggested, and the patient agreed. At 26 2/7 weeks' gestation, the patient had epidural analgesia, followed by transarterial balloon placement of the bilateral internal iliac arteries preoperatively in anticipation of massive postpartum hemorrhage. She was prepared according to protocol; however, an extra aseptic portable working table covered with 4 medium surgical drapes was created as a working space for the intubation process above her thighs. Longitudinal incisions were performed on the abdomen and uterus and the first female fetus, weighing 600 g, was delivered in breech presentation. The newborn was carefully extracted from the uterus, wrapped with a dry warm gauze pad, and placed on the working table. Delayed initial crying, weak movement, and general cyanosis were noted after delivery. Our anesthesiologist performed intubation using a 2.5-mm endotracheal tube with the newborn positioned on the working table. After securing the airway and applying positive pressure ventilation, the umbilical was clamped, and the neonate was covered in a plastic bag and brought to the warming unit for assessment by our neonatologists.

The top most medium-sized surgical drape on the working table was removed. The second twin, a male neonate, weighing 620 g, was delivered in breech presentation with delayed initial crying, weak movement, general cyanosis, and bradycardia after delivery. Similar intubation procedure was performed before clamping the umbilical cord. The 5-min Apgar score was 7 in the first neonate and 6 in the second neonate. Both neonates had grade I respiratory distress and apnea due to prematurity. At one month, the neonate exhibited a smooth respiratory pattern and stable blood pressure, and full enteral feeding was successfully achieved. Pathological examination of the placenta confirmed the diagnosis of acute chorioamnionitis. The patient was discharged on postoperative day 7 with an uneventful recovery.

Case 2

Patient B was 34 years old, G4P2SA1, pregnant at 26 2/7 weeks' gestation, and presented with massive watery vaginal discharge. She had underlying hyperthyroidism, a bicornuate uterus, and cervical incompetence, and she had laparoscopic cerclage one year before her last pregnancy. Tracing back through her obstetric history, her first pregnancy was terminated by suction curettage at 10 weeks' gestation due to blighted ovum. Her second pregnancy resulted in a dichorionic twin pregnancy with preterm delivery at 21 weeks' gestation and subsequent neonatal deaths due to extreme prematurity. The third pregnancy was delivered at 28 weeks of gestation via cesarean section due to placenta previa, premature rupture of membranes, severe fetal growth restriction, preterm labor, and antepartum hemorrhage, despite having McDonald cervical cerclage at 16 weeks' gestation and vaginal supplementation of micronized progesterone after the cerclage. After delivery, the cord was clamped and cut immediately, and the 650-g newborn was transferred to the resuscitation table for management. However, his condition deteriorated during resuscitation because of difficulties during intubation. His death was attributed to ELBW and respiratory distress syndrome shortly after birth.

At admission, cardiotocography showed irregular uterine contractions and a fetal heart rate of 160 b.p.m. with moderate variability. Sonography showed an active fetus with an estimated weight of 823 g, absence of amniotic fluid, and undilated cervix of 5 cm in length. Laboratory results showed an elevated white blood count (15,500/μL, segmented neutrophils 84.5%), and CRP level (12.8 mg/L). The urinalysis result was not significant. Presuming preterm premature rupture of membranes, atosiban and nifedipine for tocolysis, betamethasone for accelerating fetal lung maturation, and prophylactic antibiotics with ceftriaxone and metronidazole were administered. However, the patient went into labor two days later. Laboratory tests showed a persistent elevated CRP level (12.3 mg/L) and higher white blood cell count (18,100/μL, segmented neutrophils 91%); subclinical infection was highly suspected. With intravenous infusion of magnesium sulfate for fetal neuroprotection, the EXIT procedure with DCC via cesarean delivery was performed at 26 4/7 weeks' gestation. A male neonate, weighing 810 g, with Apgar scores at 1 and 5 min of 5 and 6, respectively, was delivered. He initially suffered from grade II-III respiratory distress syndrome, patent ductus arteriosus with left-to-right shunt, and anemia, but gradual feeding to full amounts and weaning of the ventilation were attempted at the age of one month. Pathological examination of the placenta confirmed the diagnosis of acute chorioamnionitis. The patient was discharged on postoperative day 5 with an uneventful recovery.

Discussion

Currently, several professional organizations, such as the International Liaison Committee on Resuscitation [3] and American College of Obstetricians and Gynecologists [4], recommended delaying umbilical cord clamping for at least 30–60 s in term and preterm infants not requiring intervention. In contrast, DCC is not suggested if the neonate is asphyxiated. Instead, the asphyxic infant should be separated from the placenta and transferred to a resuscitation table for urgent resuscitation, although this recommendation is not based on scientific or clinical evidence [3].

In this report, we applied the concept of EXIT, which involves delaying cord clamping after establishing a secured airway with adequate ventilation in ELBW infants where intubation is anticipated. Our approach allowed the anesthesiologists or neonatologists to perform the endotracheal intubation without deteriorating the neonate's condition. All three ELBW infants had an uneventful hospital course immediately after birth and in the intensive care unit during their first month.

Several lines of evidence support the feasibility of our management. First, and most importantly, maintaining the cardiovascular function and cerebral hemodynamic stability during the transition from fetal to neonatal life is critical. Ventilation is well recognized to be important to newborn resuscitation at birth, as lung aeration triggers a functional reorganization of the infant's circulation [5]. It not only increases oxygenation but also increases

the infant's heart rate and cardiac function by stimulating an increase in pulmonary blood flow. It has been suggested that the timing of umbilical cord clamping at birth has an impact on the neonate's physiological condition. Bhatt et al. investigated the effects of umbilical cord clamping before and after ventilation onset and on cardiovascular function at birth using a preterm lamb model [6]. They found that ventilation prior to cord clamping markedly improves cardiovascular function by increasing pulmonary blood flow, thus further stabilizing the cerebral hemodynamic transition throughout the early newborn period.

Another benefit of DCC after establishing a secured airway and ventilation onset is to increase the amount of blood transferred from the placenta to the infant. Similar to the effects on term infants, a recent systemic review on 12 randomized, controlled trials have documented the safety and benefits of DCC in very preterm infants (<32 weeks of gestation) [7]. These benefits include decreased mortality, fewer transfusions, better circulatory stability, and lower rates of intraventricular hemorrhage.

Furthermore, the data from clinical observation show the feasibility, safety, and benefits of ventilation during DCC in early preterm infants. In a study with a total of 62 infants delivered at or before 29 weeks of gestation, Nevill and Meyer found that infants who breathed spontaneously during DCC were less likely to have chronic lung disease and severe intraventricular hemorrhage compared with the infants who did not breathe during DCC [8]. More recently, Katheria and colleagues conducted a randomized trial to assess the effect of providing ventilation during DCC in infants delivered before 32 weeks' gestation [9]. Although there was no difference in the hematocrit level in the first 24 h of life, the onset of breathing, cardiac output, stroke volume, and cerebral oxygenation, infants with assisted ventilation during DCC received a shorter duration of stimulation during resuscitation compared with the infants receiving DCC alone.

Regarding the EXIT procedure for ELBW infants, there are some limitations and risks that merit attention. First, the umbilical cord of ELBW infants is shorter and has a smaller caliber than that of the term infants. It is, therefore, easy to separate the placenta from the uterus or tear the umbilical vessels while removing the infant from the uterus. Second, the neonatologists are usually more familiar with performing intubation on a resuscitation table, rather than using the working space created above the patient's legs. Third, there is a risk of dislodging the endotracheal tube while transferring the intubated infant to the resuscitation table. Finally, although we used warm gauze pads to wrap the newborns, there is a risk of hypothermia if the intubation takes too long because the temperature of the operating room is lower than that of a warming resuscitation table.

ELBW infants are frequently delivered by cesarean section for indications such as malpresentation, placenta previa with hemorrhage, or preterm premature rupture of membranes. When cesarean delivery is indicated, we propose delaying cord clamping after establishing a secured airway for ventilation to maintain neonatal cardiovascular stability and allow physicians to resolve the technical difficulties of endotracheal intubation.

Conflicts of interest

The authors have no conflicts of interest relevant to this article.

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